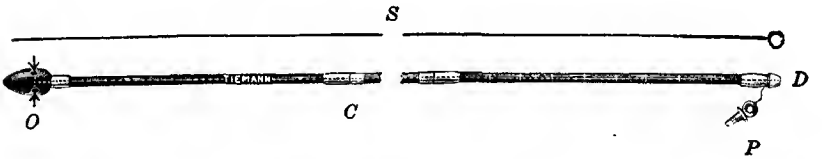
undertaken. The class of cases under consideration are often in a weakened condition, and any instrumental manipulation on them, even if done with the greatest of care, causes some discomfort.

It appeared to me, therefore, of advantage to construct an instrument which could be used for both purposes at the same time, namely, for the detection of strictures and also for obtaining fluids. The following is a description of the bougie:

The aspirating bougie resembles the usual whale-bone bougie, with the difference that the whale-bone is replaced by a canal-bearing catheter (size 14 F. twenty-four inches long), and that the olives are hollow and perforated in such a manner that fluids can easily be aspirated by a syringe. Different sized olives can be screwed on. The stem is divisible and screwed together in order to be easily handled. A wire stylet or mandrin serves to give the stem the requisite stiffness. A plug is fastened on the distal end. Before withdrawing the instrument the plug is inserted into the distal opening in order to retain any material within the olive for inspection and examination. The drawing illustrates the different parts of the instrument.



The aspirating bougie for esophagus and stomach. *O*, perforated olives of various sizes; *C*, catheter, 14 mm. in circumference and 60 cm. long; *D*, distal end; *P*, plug, attached by thread; *S*, wire stylet.

The same instrument can also be used for obtaining gastric contents in patients who cannot swallow the usual stomach tube, as it can be easily introduced without much assistance on the part of the patient. It can also be employed for fractional tests if desired.

I have used the aspirating bougie, made for me by Messrs. Tiemann & Co., with great satisfaction, and I herewith recommend it to the profession.

THE TREATMENT OF CIRCULATORY FAILURE IN ACUTE INFECTIONS.[1]

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Before we can intelligently combat the symptoms which arise in the course of acute infectious diseases connoting failure of the

[1] Read before the Hospital Graduates' Club, December 23, 1915.

circulation, it is obvious that we should have some understanding of the factors involved in such failure, and if a careful examination of the evidence derived from the experimental laboratory and from the bedside of our patients does not permit us to draw definite conclusions as to what portion of the circulatory mechanism is at fault when such symptoms present themselves, we should at least be prepared to apply our therapeutic efforts in such emergencies with rational empiricism.

In 1899 Romberg and Pässler,[2] in a series of experiments on animals, apparently demonstrated that the collapse observed in various acute infectious diseases was due to paralysis of the vasomotor center in the medulla. They based their belief on their failure to obtain any rise in blood-pressure in asphyxia occurring in pneumonia, diphtheria, septicemia, and other infections after stimulation of the nasal mucous membranes or on stimulation of the central end of the sciatic nerve.

So generally was this work of Romberg and his associates accepted and applied to the human subject suffering from an apparently similar condition, that one will find in nearly all modern theses on the treatment of circulatory failure in acute infections the statement that treatment should be aimed at the vasomotor centers rather than at the heart.

The impulse which served to start the pendulum on its swing away from Romberg's teaching was initiated by Porter[3] and his assistants. They injected animals with a lethal dose of diphtheria toxin, and then, several hours before death would probably have taken place, determined, by the average time of death in control animals, the state of the vasomotor center was tested by measuring the reflex change in blood-pressure obtained by stimulating the depressor and sciatic nerves. Stimulation of the central end of the depressor nerve caused a fall in blood-pressure averaging 36 per cent. of the blood-pressure before such stimulation, while the average rise in blood-pressure obtained after sciatic stimulation was 33 per cent., and they concluded that "the experimental evidence proves that the vasomotor center is not impaired in fatal diphtheria intoxication."

Porter and Newburgh[4] in a series of experiments on animals undertaken to ascertain the state of the vasomotor apparatus in pneumonia, demonstrated "a normal vasomotor reflex with almost wholly consolidated lungs in animals about to die," and they concluded that "experimental evidence proves that the vasomotor center is not impaired in fatal pneumonia."

Romberg and Pässler in their experiments on animals produced fatal pneumonia and diphtheria, and when the animal was near death they massaged the abdomen and caused by this procedure a

[2] Deutsch. Arch. klin. Med., 1899, lxiv, 652.
[3] Am. Jour. Physiol., xxxiii, 431.
[4] Ibid., xxxv, 1.

moderate rise in blood-pressure, and they argued that if the heart muscle was exhausted it would yield to this increase in load and no rise in blood-pressure would follow. That such a conclusion was not justified was shown later by several observers, who proved that massage of the splanchnic area would cause a rise in arterial pressure even in dead animals.

MacCallum[5] injected dogs with diphtheria toxin and found that "though the hearts from poisoned animals are rather weak and apt to be irregular, it is clear that they continue to beat for several hours after they have shown every sign of failure in the body of the dying animal if only the pressure of nutritive fluid be maintained in the coronary arteries . . . all of this seems to show fairly well that the death which occurs in the height of an attack of diphtheria is not exclusively the result of direct injury to the heart, although that may play some part in the process."

Porter and Newburg[6] demonstrated that the heart muscle of a dog which has died of pneumonia contracts as well as the heart muscle from a normal dog, provided the vessel to this muscle is fed with normal blood. They observed that pneumonia blood suddenly fed to a normal heart muscle lowers its efficiency, but that heart muscle gradually exposed to the poison adjusts itself to its poisoned food, and as a result of their experiments they conclude that the heart muscle is not functionally impaired in pneumonia. Clinical observation on the blood-pressure in pneumonia rather supports the experimental evidence produced by Porter that failure of the vasomotor center is at least not always the cause of death in cases which terminate fatally with symptoms of circulatory collapse.

Gibson formulated a rule based upon the pulse-rate and blood-pressure readings in pneumonia which he considered of important prognostic significance in this disease. The rule is that "when the blood-pressure expressed in millimeters of mercury falls below the pulse rate per minute expressed in figures the prognosis is unfavorable."

Newburgh and Minot,[7] however, have demonstrated the fact that the systolic pressure readings in some fatal cases of pneumonia tend to be higher than in those which recover, and in applying Gibson's rule, found that the rule obtained in but 43 per cent. of the cases observed, and they concluded that:

1. The blood-pressure curve does not suggest failure of the vasomotor center in pneumonia.
2. Low systolic pressures are not invariably of evil omen.
3. Blood-pressure measurements cannot be used as a basis for treatment.

There is nothing to justify the assumption that the heart is entirely at fault in the presence of symptoms of circulatory failure

[5] Am. Jour. Med. Sc., cxlvii, 37.
[6] Jour. Exp. Med., xxii, 123.
[7] Arch. Int. Med., xiv, 48.

occurring in the course of acute infections, nor, on the other hand, is there sufficient clinical or positive experimental evidence to permit one to exclude the heart as a factor at least in such failure.

The symptoms which we have been in the habit of ascribing to failure of some portion of the circulatory mechanism in human beings suffering from acute infectious diseases are, briefly: cyanosis; dyspnea; a rapid pulse, rapid out of proportion to the height of the fever; or a pulse-rate which is increasing while the temperature is falling; a sudden fall in blood-pressure; increase in the area of cardiac dullness, especially to the right; a failing first sound at the apex or a diminution in the intensity of the second sound over the pulmonary area; cardiac irregularities; and pulmonary edema.

It has been generally believed that the circulation in the body is maintained chiefly by two factors: the force of the heart as a pump and the peripheral resistance in the vessels maintained by the contraction of the small arteries, which in turn are in a measure controlled by an active vasomotor center in the medulla; but in the light of our present knowledge concerning the integrity of the vasomotor centers in acute infections and in the absence of positive proof that the myocardial efficiency is impaired in such conditions, it seems possible at least that there is a *tertium quid*, a third something, operating outside the heart and vasomotor centers, though more or less intimately associated with them, which controls the flow of blood.

The balance between the circulation and respiration is maintained by conditions existing in the blood. The action of the blood on the respiratory mechanism is not due to CO_2 alone, but also to the presence in the blood of non-volatile acids; and it does not seem probable that one part of the respiratory mechanism, the ventilation of the lungs, is delicately balanced, while the other mechanism, the circulation of the blood, is not so balanced; and Boothby suggests that the factor which regulates respiration and governs the ventilation of the lungs also governs the circulation of the blood.[8] Porter has recently questioned the generally accepted theory that both the vasomotor reflexes and the arterial tonus are controlled by the same center, the vasomotor center, and suggests the possibility of the existence of a vasotonic and vasoreflex center related but separable.[9] Boothby's work suggests the possibility of a combination of a subordinate circulatory center and a ventilation center.

In the rational treatment of a pathological process we must recognize not only the necessity for intelligent management of complications which may arise in the course of such a process, but we must also have a keen appreciation of those procedures which may be instituted in order that such complications may be antici-

[8] Jour. Am. Med. Assn., lxv, 959. [9] Ibid., lxiv, 1659.

pated and possibly prevented. So in a discussion of the treatment of circulatory failure it is necessary to emphasize those factors which are unfavorable to the maintenance of good circulation.

The importance of rest to the patient is perfectly obvious. In the management of any diseased condition, modern therapeutic effort seeks to spare bodily function, and rest in acute infections means circulatory prophylaxis in its very broadest sense. So we select for our patient a comfortable bed that he may obtain the greatest degree of muscular relaxation. We endeavor to relieve his cyanosis, dyspnea, and nervous manifestations by giving him fresh, circulating, and, if possible, cold air. We seek to relieve, by appropriate measures, excessive or unproductive cough, to combat tympanites when it occurs, to relieve excessive pain, and to promote quiet and restful sleep by every means possible. Careful attention to such details constitutes a very important part of the effort we should make to conserve the efficiency of the entire circulatory mechanism.

Tradition must play no part in dictating to our therapeutic judgment in the selection of various drugs by means of which we endeavor to combat the symptoms of circulatory failure when they have occurred, and I say this with a very full appreciation of the necessity for empiricism even in present-day treatment. The drugs which I have chosen to discuss are: alcohol, strychnin, camphor, epinephrin, pituitary extract, the nitrites, and digitalis.

Alcohol. Delafield in his lectures on pneumonia and diphtheria says: "The heart failure is of the same character that we get in any of the severe infectious diseases." . . . "It requires the ordinary management with alcohol and cardiac stimulants."

Janeway[10] says: "Least of all of the so-called stimulants does alcohol deserve the name. It is without influence on blood-pressure or the force of the heart in animals, normal men or diseased conditions."

And these two statements admirably represent the difference, as far as this drug is concerned, between the therapy of twenty years ago and the present-day therapy.

I am loath to discard any of the teachings of that master mind in medicine, Dr. Delafield, for he was a keen observer, and most of the statements made by him years ago hold good for today; but alcohol today is not considered to stimulate any portion of the cardiovascular system—indeed, there is much evidence that it does just the contrary. I am speaking of alcohol now purely from the stand-point of its effect on the circulation. It may do good in relieving active delirium; in fact, I believe that it does; but it is of value here because of its depressant effect on the higher centers already overstimulated by the toxemia of the disease and not

[10] Clinical Study of Blood-pressure, 223.

because it stimulates the circulation. Alcohol causes dilatation of the skin vessels after moderate doses. Large doses cause a fall in blood-pressure; the heart-rate is not changed by therapeutic doses.

Lieb[11] in an effort to determine the reflex effects of alcohol on the circulation found that moderately strong alcohol taken by the mouth produces local irritation of the gastric mucous membrane. Such irritation produces a rise in blood-pressure and an accelerated heart; but if alcohol is given well diluted by the mouth it causes no local irritation, and there is, in consequence, no rise in blood-pressure. Lieb gave cats doses of alcohol varying from 0.5 c.c. to 5 c.c., and in no case was there any change in heart-rate or blood-pressure within half an hour of its administration. He made forty-three observations on twenty-one different patients suffering from various acute infections, typhoid, pneumonia, rheumatism, malaria, etc.

In one patient alcohol was given at a time when circulatory stimulation was called for, yet alcohol not only did not produce any improvement, but, on the contrary, it actually decreased the efficiency of the circulation.

Lieb believes that in the presence of severe toxemia, alcohol loses its power to raise blood-pressure even reflexly. He says: "Advocates of the use of alcohol may claim that alcohol improves the circulation in some fashion other than raising blood-pressure or increasing the heart-rate." It may increase the velocity of the flow or it may improve the efficiency of the heart as a pump; but in applying Tigerstedt's formual $V\frac{PP \times PR}{SP \times PR}$, Lieb showed that the changes induced by alcohol in these factors was very slight; in fact, the efficiency of the heart as a pump was decreased.

His conclusions with his experiments as a basis were that "Even though alcohol may raise for a few moments the systolic blood-pressure, and thus act as an apparent circulatory stimulant, it cannot be regarded as a true circulatory stimulant, inasmuch as it decreases cardiac efficiency, raises disproportionately the diastolic-pressure, and lowers pulse-pressure." And in my opinion this statement just about represents the value of alcohol as a cardio-vascular stimulant.

STRYCHNIN is another drug which enjoys a considerable reputation as a circulatory stimulant. Tradition and tradition alone is responsible for its use as such. Vague expressions as to its clinical value, estimated by the feel of the pulse, the subjective improvement of the patient, are frequent in medical literature in this country and to some degree in England. Little is seen in the German and French literature of its use for this purpose. It has never been shown that strychnin does or can relieve cardiac failure. As keen

[11] Jour. Am. Med. Assn., lxiv, 898.

an observer as Mackenzie says of it: "I have carefully sought for its special effect on the heart and found none."

Newburgh[12] in his experiments on patients with this drug shows that "none of the patients were benefited by strychnin; compensation was not improved in the slightest," and he concludes that "neither pharmacological nor clinical evidence justifies the use of strychnin in the treatment of acute or chronic heart failure."

Pilcher and Sollmann[13] show that therapeutic doses of strychnin have no direct effect on the heart. There is no action on the blood-vessels directly. It produces no marked or constant effect on blood-pressure, and they conclude that doses of strychnin large enough to be dangerous (0.05 mg. per kilo) are "usually without action on the vasomotor center, but may stimulate the center moderately."

Parkinson and Rowlands,[14] in England, found no evidence that strychnin used subcutaneously in full doses in cases of cardiac failure produced any change in blood, the blood-pressure, rate of pulse, rate of respiration, or general symptoms within an hour after administration, and concluded that strychnin has no effect which justifies its employment as a cardiac stimulant.

Newburgh[15] showed that strychnin sulphate in medicinal dosage does not increase the output of the heart.

It is, of course, true that the empiric use of drugs is occasionally beneficial; but here is a drug which has been praised as a cardiac stimulant by some observers that fails absolutely to produce results in cardiac failure, and in cases too that responded, after its use, immediately to digitalis in the ordinary manner.

With such weight of evidence against its value, surely we must admit that it is at least a very slender reed to tie to in case of such dire need as often presents itself in the circulatory failure of such diseases as we are discussing.

Camphor has more to recommend it in the circulatory failure of the acute infectious diseases than either alcohol or strychnin, but since I have said that these two drugs are absolutely valueless, I fear that my statement with reference to camphor condemns it with faint praise. Edsall and Means[16] in a series of experiments carried out in human beings to determine the effect of various drugs on the respiration and respiratory metabolism, concluded that "the results obtained with camphor show no constant effect. In one experiment there was a slight fall in CO_2 tension, suggesting that there may have been some stimulation of the center, but in the other experiments there was none. Circulation rate and respiration rate are essentially unaltered."

[12] Am. Jour. Med. Sc., cxlix, 696.
[13] Jour. Pharmacol. and Exp. Ther., vi, 331.
[14] Quart. Jour. Med., vii, 42.
[15] Arch. Int. Med., xv, 458.
[16] Ibid., xiv, 897.

Heard and Brooks[17] in clinical experiments with camphor injected subcutaneously in oil in doses up to 50 grains failed to produce any definite effect.

Plant[18] in his experiments with the effects of camphor on the normal isolated dogs' heart muscle failed to produce any distinct and constant stimulation.

Pilcher and Sollmann[19] in their experimental work with the effects of drugs on the vasomotor center concluded as to camphor that in therapeutic doses it is probably without action on this center.

I am perfectly willing to admit that the centers may be more easily influenced when depressed by disease than when in the normal state.

I have used camphor as a stimulant in acute fevers with symptoms of circulatory failure, and I have thought that it did good, but there are other drugs of much more certain practical and theoretical value.

EPINEPHRIN is fleeting in its action, and in consequence should not be prescribed when sustained effect on the circulatory mechanism is desired. Epinephrin when injected intravenously or intermuscularly causes a prompt rise in blood-pressure, due to the direct action of the drug on the muscles of the vessel wall or on the terminations of the nerves in them.

The heart is at first accelerated and then slowed, the acceleration being due to stimulation of the accelerator fibers in the heart muscle, and the heart, in consequence, contracts more strongly and more completely.

The slowing of the heart is a vagal effect, not direct, but incidental and subsequent to heightened blood-pressure. It has no direct effect on the vasomotor apparatus, but frequently there may be slight stimulation of this center, secondary to the rise in blood-pressure.

Experimental evidence produced by Barbour and Prince[20] shows that epinephrin has the same effect on the coronary vessels of the heart in man as the members of the digitalis group, excepting digitonin—that is, it causes constriction of these vessels.

Epinephrin is, therefore, indicated when there is evidence of acute circulatory collapse with falling blood-pressure and rapid pulse. Janeway,[21] in an article on "The Comparative Value of Cardiac Remedies," says: "I have seen the most amazing restoration from apparent imminent death follow the intravenous injection of epinephrin in large doses; in one case over 4 c.c. of 1 to 1000 solution in a little more than one hour. This was in a case of pneumonia with extreme cyanosis. Life was prolonged for three days."

There is every evidence, experimental and clinical, to warrant

[17] AM. JOUR. MED. SC., cxlv, 238.
[18] Jour. Pharm. and Exp. Ther., v, 571.
[19] Ibid., vi, 345.
[20] Jour. Exp. Med., xxi, 330.
[21] Loc. cit.

the use of epinephrin in acute circulatory collapse occurring during the course of such an acute infection as pneumonia. Indeed, in spite of its fleeting action, one may tide his patient over a circulatory crisis and actually save life by its use.

A word of caution is necessary concerning the age of the preparation of epinephrin to be used. Apparently a product which has been exposed for some time loses its constrictor effect, but not its dilator, and a fall in pressure instead of a rise may take place after the intramuscular or intravenous use of such a preparation.[22]

PITUITARY EXTRACT of the infundibular portion of the pituitary gland has an action very similar to that of epinephrin, the difference between the two being rather a matter of intensity than of kind. Blood-pressure is raised, but not so rapidly nor so high as after adrenalin; but the effect lasts for a much longer time. The blood-pressure is raised by direct action on the bloodvessels. Pilcher and Sollmann[23] demonstrated that in animals it had no effect on the vasomotor centers.

The indications for its use are the same as those enumerated under adrenalin, with the addition possibly of its value in the treatment of tympanites when by stimulating the paretic intestinal muscles it often relieves distention, and in consequence the heart is relieved of an important mechanical element favoring failure of the circulation.

THE NITRITES, *i. e.*, nitroglycerin, amyl nitrite, and sodium nitrite, have a distinct place in the therapeutic armamentarium of the physician called upon to treat one type at least of cardiovascular failure occasionally seen in acute infections, more often perhaps in lobar pneumonia than in other infections, namely, pulmonary edema.

The nitrites cause direct peripheral depression of the arterioles, with a consequent fall in pressure. The vasomotor center is never depressed in animals by the use of the nitrites. In fact, Pilcher and Sollmann[24] proved that stimulation was the rule. Such stimulation probably is due to the anemia of the centers caused by the dilatation of the peripheral vessels.

Another important observation made by Macht[25] is the effect of the members of this group on excised strips of medium-sized pulmonary arteries. The nitrites caused constriction of the pulmonary strip. This action of the nitrites is corroborated by other experimental data, and the explanation of such action is that the pulmonary artery is richly supplied for the most part with vasoconstrictor nerve terminals. It is this selective action of the nitrite group of drugs which makes them valuable in the treatment of some cases of pulmonary edema.

[22] Jour. Am. Med. Assn., lxiv, 1396.
[23] Jour. Pharm. and Exp. Ther., vi, 405.
[24] Ibid., vi, 323.
[25] Ibid., vi, 13.

CAFFEIN. The effects of caffein on the circulation have been studied both pharmacologically and clinically by several workers during the past two years. Pilcher and Sollmann[26] found in experiments conducted upon animals that caffein caused vasodilatation with sufficient cardiac stimulation to maintain or even somewhat increase blood-pressure.

These actions favor flow, and I shall refer presently to work done by Means and Newburgh to show that it does increase the flow of blood in human beings. This is certainly a highly desirable effect in circulatory disturbance.

Pilcher and Sollmann conclude, as a result of their experiments on animals, that caffein causes: (1) cardiac stimulation; (2) increase in heart rate which is not due to vagus depression; (3) vasodilatation through peripheral depression of the vasoconstrictor mechanism; (4) central vasoconstrictor stimulation is generally ineffectual.

The acceleration in the heart-rate is probably due to direct action of the drug on the heart muscle.

While Edsall and Means,[27] Lucas,[28] and later Newburgh[29] noted little or no effect on blood-pressure, or on the rate or character of the pulse, from caffein administered in therapeutic doses to patients suffering from acute infectious diseases with or without low blood-pressure, Means[30] and Newburgh report an extremely interesting and important series of experiments conducted on human beings in order to determine the effects of caffein on the blood-flow in normal human beings. Their method consisted in determining the rate of absorption of nitrous oxide gas in the lungs. Nitrous oxide gas forms no chemical combination with hemoglobin, but goes into physical solution in blood plasma, so according to a definite coefficient it was possible to calculate how much blood must have passed through the lungs in order to absorb a measured amount of nitrous oxide gas from an original mixture of known concentration.

The blood-flow as determined by this method is, of course, that flowing through the lungs or from right to left heart. There is a marked variation in blood-flow during rest, and this is due to the fact that during rest the supply of blood is "inadequate" to fill the ventricles to their utmost capacity during each diastole; under such circumstances the output of the heart is dependent upon the supply of venous blood and is not directly related to the functional capacity of the heart. During work the flow of blood shows less variation; in other words, "during work the supply of blood to the heart becomes adequate." They showed that during rest or when

[26] Jour. Pharm. and Exp. Ther., iii, 89.
[27] Arch. Int. Med., xiv, 897.
[28] Am. Jour. Dis. Child., vii, 208.
[29] Arch. Int. Med., xv, 458.
[30] Jour. Pharm. and Exp. Ther., vii, 449.

the supply of venous blood is "inadequate," caffein frequently causes a rise in total blood-flow, and often this increase occurs without corresponding rise in pulse-rate. During work no action was obtained from caffein other than an increase in pulse-rate, and consequently there was a slight diminution in systolic output. They suggest in conclusion that during rest or when the flow of blood to the right heart is "inadequate," caffein increases the flow by increasing the venous supply through action on some mechanism outside the heart, when the supply becomes "adequate" or approaches adequacy no such action is obtained.

DIGITALIS and the other members of this group of drugs is, according to some observers, of little value in the treatment of circulatory failure occurring in the course of acute infectious diseases.

Mackenzie says that "I have never seen much good follow the administration of digitalis in acute febrile conditions;" and again, "Digitalis will be found to be of little value when the heart is already in the grip of some poison, whether it be the specific organism of such diseases as rheumatism, pneumonia, etc., or the toxins of such diseases or such poisons as alcohol."

Gibson says that "In the worst cases of pneumococcal poisoning the heart refuses to respond to digitalis."

Janeway believes that "Digitalis given by the mouth in these cases is worthless." Krehl, on the other hand, believes it to be beneficial.

Just what is meant by the failure of digitalis to act in the presence of fever is not altogether clear. If a reduction in rate is the action expected in this type of case, one can understand why it is said to be of no value. The most decided effects on rate after digitalis administration are noted either in those cases in which the normal pacemaker is eliminated, as in cases of auricular fibrillation, or in those cases with a normally functioning sinoauricular node in the presence of edema.

In view of the work of Cohn[31] in an electrocardiographic study on the action of digitalis it seems probable that slowing the rate of the heart is not at least a "primary function of digitalis." He showed in individuals with a regular rate that digitalis caused a definite lengthening of the conduction time between auricle and ventricle, and also that it produced a distinct "alteration in the size, shape, and direction of the T-wave in the electrocardiogram. These effects were produced in persons with perfectly normal hearts, and even in the absence of any effect on rate. Precisely the same effects were noted in febrile cases, thus proving that whatever its nature the "same sort of support can be given the heart by digitalis during fever as in its absence."

[31] Jour. Am. Med. Assn., lxv, 1527.

In febrile cases showing abnormal rhythm, such as fibrillation and flutter, precisely the same effects on rate were noted after the administration of strophanthin intramuscularly or digitalis by the mouth as obtain in similar conditions occurring in non-febrile states.

Jamieson[32] as a result of his experiments on animals undertaken for the purpose of ascertaining whether the action of a digitalis body when administered to animals suffering from pneumonia differed in its action when no infection or fever was present, concluded:

1. When a like amount of strophanthin is injected intravenously, the mortality is the same in both normal cats and in cats suffering from induced pneumonia.

2. The presence of an acute infection in these animals does not interfere with the action of strophanthin on the heart.

3. The identity of strophanthin action in infected and normal animals renders it probable that a like similarity may be anticipated in man under normal conditions and in pneumonia.

Gunn[33] in his experimental work conducted in animals to demonstrate the influence of temperature on the action of strophanthin on the mammalian heart, showed at least high fever is not the cause of failure of action of digitalis, and that if the heart does not respond to digitalis bodies, it is probable that the heart is in a refractory state from the presence of toxins.

Sollmann, Mendenhall and Stingel[34] agree in the main with Gunn, for they proved that in animals at least ouabain or crystalline strophanthin acts more quickly on the isolated rabbit's heart as the temperature of the animals is raised.

CONCLUSIONS. 1. There is neither clinical nor experimental evidence to support the belief that failure of the vasomotor center is the cause of the symptoms of circulatory failure which occur in acute infectious disease.

2. While it has been shown experimentally that the heart is not exhausted in animals dying of acute infectious diseases, there is no positive proof that the myocardium is wholly efficient in its effect to maintain the circulation in the body of the living animal under such circumstances.

3. The hypothesis which suggests the existence of a third center controlling the flow of blood is important even though it is not yet proved.

4. Alcohol and strychnin are absolutely worthless drugs in the treatment of circulatory failure.

5. Epinephrin and pituitary extract are useful in the treatment of sudden circulatory collapse, but their action is not a sustained one.

[32] Jour. Exp. Med., xxii, 629.
[33] Jour. Pharm. and Exp. Ther., vi, 39.
[34] Ibid., vi, 533.

6. The nitrites are valuable additions to our therapeutic armamentarium in the treatment of pulmonary edema under certain circumstances, because of their selective action in constricting the pulmonary arteries.

7. Caffein increases the flow of blood when the supply to the heart is "inadequate," probably by an action on some mechanism outside of the heart.

8. One of the most important contributions of recent times on the action of digitalis is the proof electrocardiographically that it exerts precisely the same effect on the heart in febrile conditions that it exercises in non-febrile states, and whether the rhythm is initiated in the normal pacemaker or not.